The International Association for the Study of Lung Cancer Lung Cancer Staging Project

Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer

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Introduction: Nodal status is considered to be one of the most reliable indicators of the prognosis in patients with lung cancer and thus is indispensable in determining the optimal therapeutic options. We sought to determine whether the current nodal (N) descriptors should be maintained or revised for the next edition (8th) of the International Lung Cancer Staging System.

Methods: The new International Association for the Study of Lung Cancer lung cancer database was created from 94,708 patients diagnosed as having lung cancer between 1999 and 2010. Among these, 38,910 and 31,426 patients with non–small-cell lung carcinoma were available for an analysis of the clinical (c)N and pathological (p)N status, respectively. The anatomical location of lymph node involvement was defined by either the Naruke (for Japanese data) or American Thoracic Society (for non-Japanese data) nodal charts. Survival was calculated by the Kaplan–Meier method, and prognostic groups were assessed by a Cox regression analysis.

Results: The current N0 to N3 descriptors for both the cN and pN status consistently separated prognostically distinct groups. The 5-year survival rates according to the cN and pN status were 60% and 75% (N0), 37% and 49% (N1), 23% and 36% (N2), and 9% and 20% (N3), respectively. The differences in survival between all neighboring nodal categories were highly significant for both the cN and pN status. With regard to pathological staging, additional analyses regarding the prognosis were performed by further dividing N1 into N1 at a single station (N1a) and N1 at multiple stations (N1b); N2 into N2 at a single station without N1 involvement ("skip" metastasis, N2a1), N2 at a single station with N1 involvement (N2a2), and N2 at multiple stations (N2b). The survival curves for N1b and N2a2 overlapped each other, and N2a1 had numerically a better prognosis than N1b, although the difference was not significant. Geographic difference in N-specific prognosis was observed for both c-settings and p-settings. This might have been because of the difference in the used nodal map, surgical technique, and pathologist's handling of the resected specimen.

Conclusions: Current N descriptors adequately predict the prognosis and therefore should be maintained in the forthcoming staging system. Furthermore, we recommend that physicians record the number of metastatic lymph nodes (or stations) and to further classify the N category using new descriptors, such as N1a, N1b, N2a, N2b, and N3, for further testing.

Key Words: Lung cancer, Lung cancer staging, N component, N descriptors, Tumor, node, metastasis classification, Lymph node metastasis.

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The cancer staging classification describes the anatomical extent of malignant tumors in terms of three components: primary tumor (T), nodal status for metastasis (N), and

metastasis at the distant organs (M). The TNM classification has been revised periodically by both the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) for epithelial and nonepithelial solid tumors of various organs.[1,2] For most organs, a revision is proposed by the AJCC to the UICC as an agenda item created by the "organ task force" of the AJCC. However, lung cancer has a unique process of revision, in which the International Association for the Study of Lung Cancer (IASLC) has taken the initiative to develop proposals for revisions based on a newly collected large data set of their own and meticulous statistical analyses. This truly global, multidisciplinary effort has been termed the "IASLC Lung Cancer Staging Project"[3] and was responsible for creating the 7th edition of the TNM staging system for lung cancer.[4] The changes proposed by the IASLC were fully approved by both the UICC and the AJCC and are reflected in the current 7th edition of the TNM staging system for lung cancer. The 7th edition is currently in the process of being revised into the 8th edition.[3] This article presents the results of analyses on a newly established database for the specific revision of the N component as a part of the IASLC Lung Cancer Staging Project.

In the 7th edition, lymph node involvement in lung cancer is categorized according to the location of the metastatic lymph nodes as N0 (no nodes involved), N1 (ipsilateral peribronchial, interlobar, or hilar node involvement), N2 (ipsilateral mediastinal node involvement), or N3 (contralateral mediastinal, contralateral hilar, or supraclavicular node involvement).[1,2] The UICC and AJCC in the 7th edition of TNM for Lung Cancer accepted the IASLC Nodal Map and anatomical definitions as the recommended means of describing regional lymph node involvement for lung cancers. Thus, lymph node metastasis in lung cancer has been graded in terms of the location of involved lymph nodes regardless of the number of involved lymph nodes. In the revision of the 6th to the 7th edition, nodal categorization defined as N0, N1, N2, and N3 remained unchanged because it was highly prognostic.[5]

The purpose of this study is to see whether the present N categorization accurately reflects the prognosis, to explore if there is a more sophisticated method for describing the tumor burden in lymph nodes, using a newly established database, and to conclude whether the present nodal descriptors should be maintained or revised.

METHODS

Data Acquisition and Analysis (The IASLC Lung Cancer Staging Project)

The process for data acquisition and analysis of the IASLC Lung Cancer Staging Project database has been described elsewhere.[3] This database was newly created for the revision of the current 7th edition of the TNM staging system for lung cancer to the forthcoming 8th edition. The characteristics and sources of the whole population of the present staging project have been described in detail elsewhere.[3] In brief, the new database for the revision toward 8th edition consists of 94,708 patients who were diagnosed with non–small-cell lung cancer (NSCLC) and small-cell lung cancer from 1999 to 2010. This databases was composed of established databases from various sources (90,041 patients) and cases from an electronic data capture system developed by Cancer Research And Biostatistics in Seattle, WA (4667 patients). The geographic distribution of the origin of the data was as follows: 46,560 patients from Europe, 41,705 from Asia, 4660 from North America, 1593 from Australia, and 190 from South America. These new data came from 35 sources in 16 countries. Among these patients, 17,552 with an unknown or different histology and incomplete stage information were excluded, and the remaining 77,165 patients (70,976 patients with NSCLC and 6189 with small-cell lung cancer) were used as subjects for further analyses.

Among 70,976 patients with NSCLC, data on the "N component" were available in 38,910 (54.8%) patients for cN status and in 31,426 (44.3%) patients for pN status. The data source and the distribution of the cN and pN status are shown in Tables 1 and 2, respectively. Japan submitted the most data, which consisted of 23,012 (59.1%) patients for cN status and 23,463 (74.7%) patients for pN status, in which the "Naruke-Japanese map" was exclusively used to designate the location of metastatic lymph nodes and to determine the nodal status.[6] In the rest of the world, the Mountain–Dresler modification of the American Thoracic Society (MDATS) was mainly used.[7] In 2009, the new international lymph node map (IASLC map) was promulgated by the IASLC as a part of the

TABLE 1. Origin of the Data for Clinical Nodal (cN) Categories

	Clinical N					Follow-up (mo)		
Data Source	**N0**	**N1**	**N2**	**N3**	**Total**	**Min**	**Median**	**Max**
Denmark	6435	845	2690	1390	11,360	4	27	124
EDC	1243	182	402	277	2104	<1	22	125
Japan 1999	8497	918	1540	79	11,034	1	66	83
Japan 2002	450	200	725	391	1766	1	16	87
Japan 2004	8501	683	985	43	10,212	1	62	88
MSKCC	535	97	198	31	861	1	80	122
Prince Charles	88	13	24	6	131	28	34	39
Sydney	14	1	3	0	18	49	59	98
TurkeyG	563	168	577	116	1424	<1	65	73
Total	26,326	3107	7144	2333	38,910	<1	61	125

EDC, electronic data capture.

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TABLE 2. Origin of the Data for Pathological Nodal (pN) Categories

	Pathological N					Follow-up (mo)		
Data Source	N0	N1	N2	N3	Total	Min	Median	Max
Belgrade	10	54	24	0	88	6	42	70
EDC	1002	218	189	21	1430	<1	23	125
Japan 1999	7717	1296	1855	100	10,968	1	66	83
Japan 2002	2994	386	401	11	3792	1	73	90
Japan 2004	6662	726	1296	19	8703	1	62	77
Korea	933	270	222	1	1426	60	87	139
MDACC	1233	260	212	0	1705	<1	42	120
MSKCC	451	74	60	1	586	1	79	110
Norway	1193	369	145	1	1708	8	55	96
Sydney	743	158	118	1	1020	<1	69	139
Total	22,938	3811	4522	155	31,426	<1	64	139

EDC, electronic data capture; MDACC, M. D. Anderson Cancer Center; MSKCC, Memorial Sloan-Kettering Cancer Center.

activities of the IASLC Lung Cancer Staging Project for the 7th edition, but it was seldom used for the cases in the present database.[8] More precisely, surgical cases from Japan were staged according to the Naruke lymph node map adopted by the Japan Lung Cancer Society as the official staging map. Many surgical cases from other countries seemed to be staged according to MDATS. There are some differences in the definition of lymph node stations near the border between N1 and N2 lymph node regions.[8] The main discrepancy between the two lymph node maps is that the Naruke map considers lymph nodes in the subcarinal space along the inferior border of the main stem bronchus to be station 10 (hence, N1), whereas these are considered as station 7 (and, therefore, N2) in the MDATS map. This difference in the anatomical definition of each lymph node station might have influenced the nodal categorization. However, with the database collected, there was no way to reasonably reconcile or amend such discrepancies.

Statistical Methodology

Survival was measured from the date of diagnosis for clinically staged data and from the date of surgery for pathologically staged data. Survival analyses were performed according to clinical and pathological nodal categories regardless of the T category and also within the different T categories. In addition, survival was analyzed according to the number of involved pathological nodal stations. For this staging project, the information on the number of metastatic nodes, not stations, was not provided outside of the cases submitted through the electronic data capture. Survival was calculated by the Kaplan–Meier method. Prognostic groups were assessed by a Cox regression analysis adjusted for histopathological type, sex, age, and geographic region, using the SAS System for Windows, version 9.2.

RESULTS

Overall Survival According to Clinical N (cN) Categories

Data on overall survival and cN status were available for 38,910 T-any M0 patients. Figure 1 shows the overall survival for all cases according to the clinical N category. The 5-year survival rates by cN status were 60% (N0), 37% (N1), 23% (N2), and 9% (N3). For all comparisons, the differences in survival between neighboring cN statuses were statistically significant (between cN0 and cN1, $p < 0.0001$; between cN1 and cN2, $p < 0.0001$; between cN2 and cN3, $p < 0.0001$). Survival according to the cN status was further analyzed within each T category (T1–4, Fig. 2). Within each T category, the different cN categories showed a difference in prognosis, especially neighboring cN statuses, for T1 and T2 tumors. In the T3 and T4 tumors, cN1 was not statistically different from cN0. However, the comparisons between cN1 and cN2, as well as between cN2 and cN3, were significant.

Overall Survival According to Pathological N Categories

Data on overall survival and pN status were available for 26,326 T-any M0 patients. Figure 3 shows the survival curves of patients with complete or incomplete resection (any R resection) and those with complete (R0) resection only. For both of these different R settings, the differences in survival

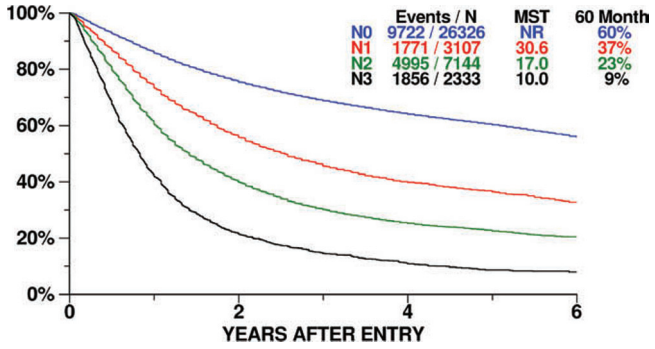

FIGURE 1. Survival curves for cN0, cN1, cN2, and cN3, T-any M0 tumors. The differences of survival between neighboring categories are all statistically significant (*p* values: between cN0 and cN1, $p < 0.0001$; between cN1 and cN2, $p < 0.0001$; between cN2 and cN3, $p < 0.0001$).

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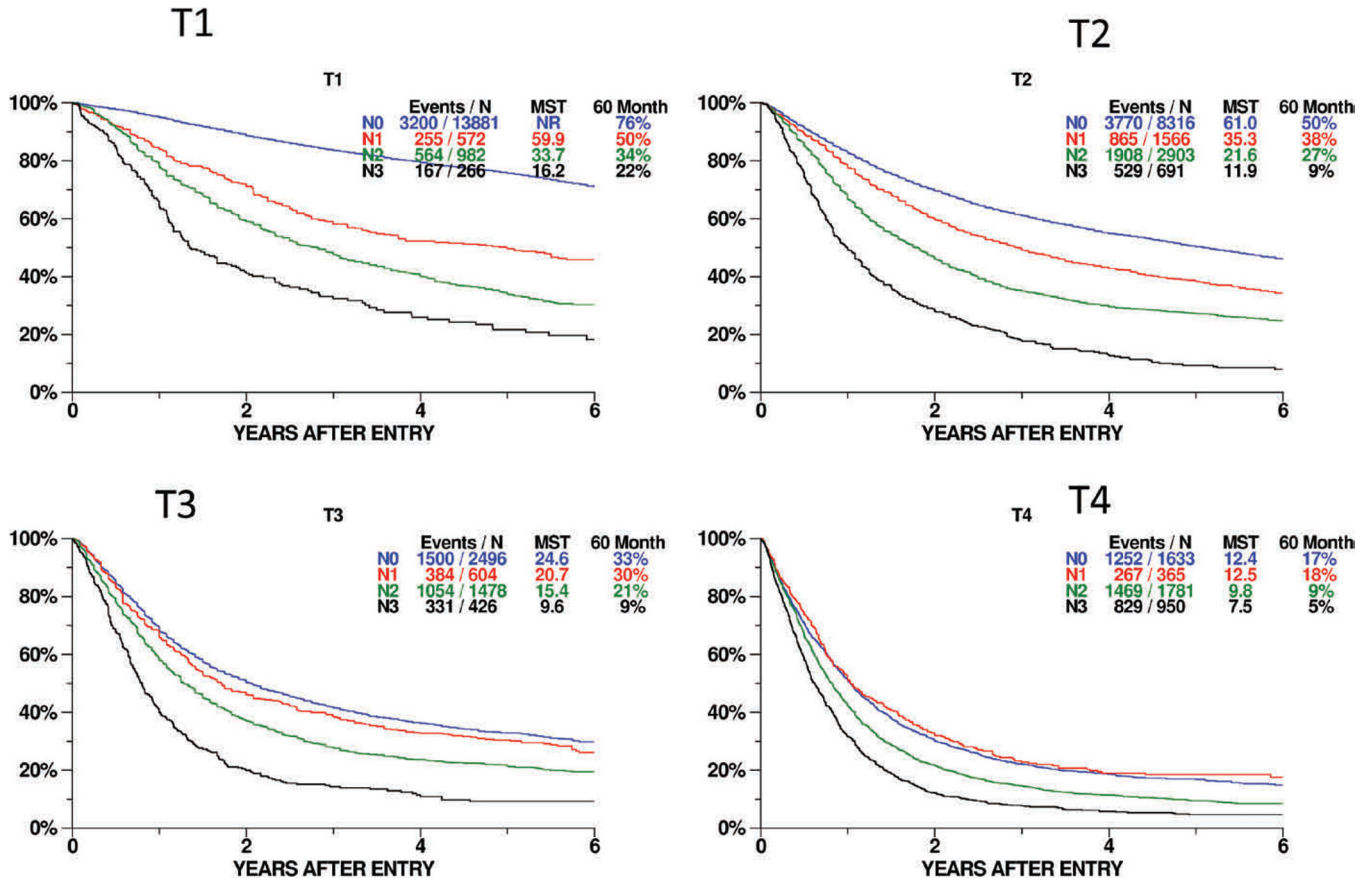
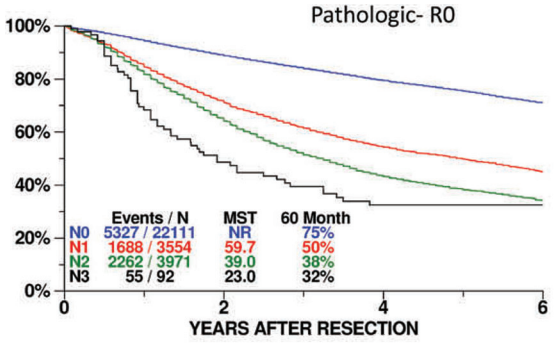
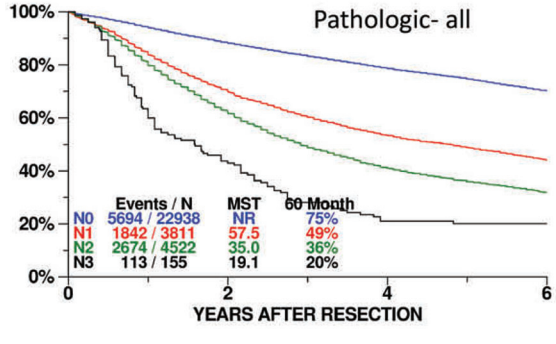


FIGURE 2. Survival curves for cN0, cN1, cN2, and cN3 according to T categories (T1–4). The differences in survival between neighboring categories are all statistically significant.



N0 vs N1 vs N2 vs N3 Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+, and Region. (Cox PH regression on R0 cases)		
comparison	HR	P
N1 vs N0	2.13	<0.0001
N2 vs N1	1.65	<0.0001
N3 vs N2	1.56	.0012



N0 vs N1 vs N2 vs N3 Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+, R0 resection, and Region. (Cox PH regression on all cases)		
comparison	HR	P
N1 vs N0	2.10	<0.0001
N2 vs N1	1.63	<0.0001
N3 vs N2	1.66	<0.0001

FIGURE 3. Survival curves for pN0, pN1, pN2, and pN3, T-any M0 tumors according to R0 and any R settings. For both settings, the differences in survival between neighboring categories are all statistically significant (for a R0 setting: between pN0 and pN1, $p < 0.0001$; between pN1 and pN2, $p < 0.0001$; between pN2 and pN3, $p = 0.0007$, for any R setting: between pN0 and pN1, $p < 0.0001$; between pN1 and pN2, $p < 0.0001$; between pN2 and pN3, $p < 0.0001$).

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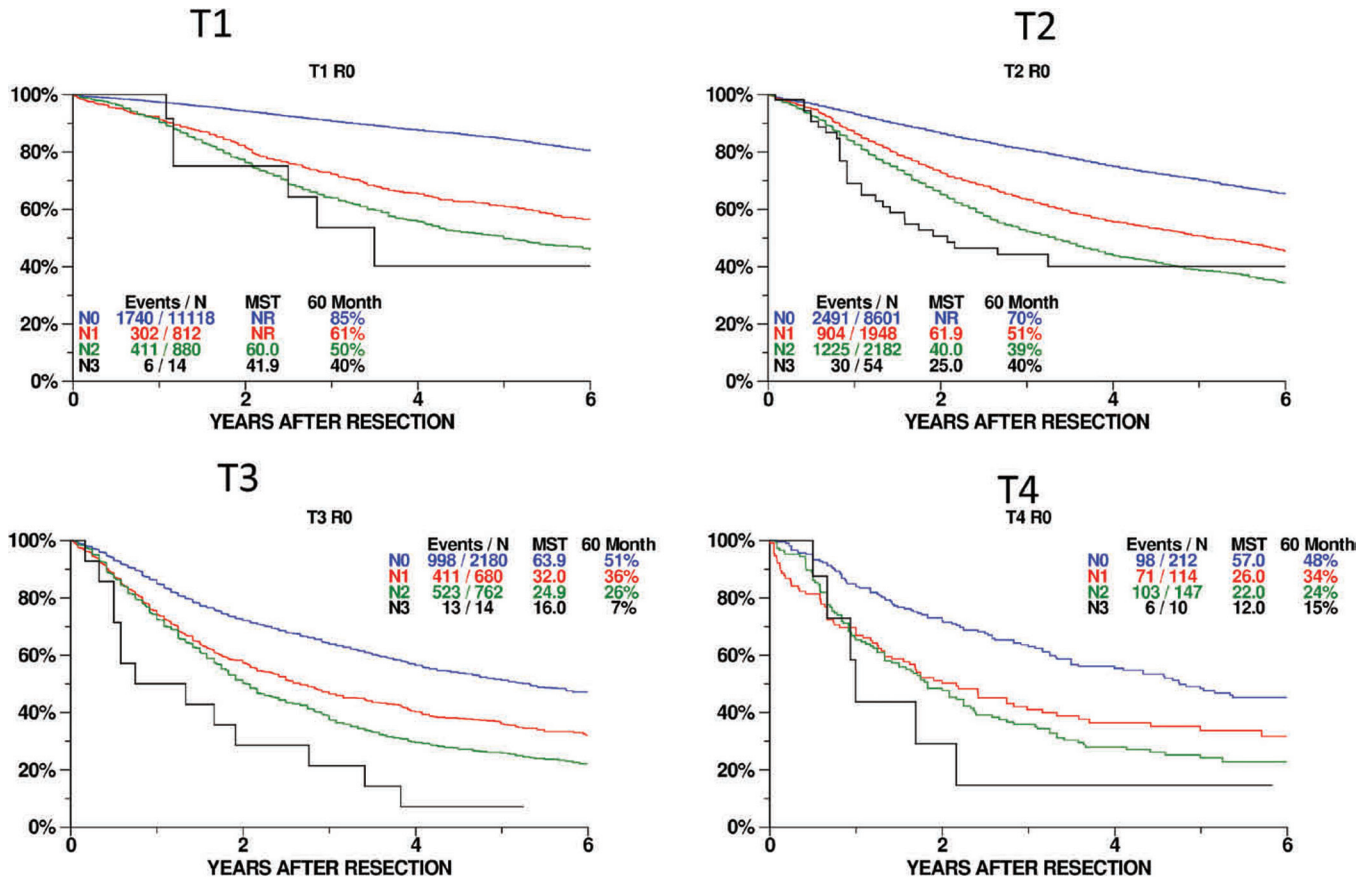

FIGURE 4. Survival curves for pN0, pN1, pN2, and pN3 in T1–4 M0 R0 resected tumors. The differences in survival between neighboring categories are all statistically significant. In T4, the differences in the survival curves among the neighboring pN categories are diminished.

between neighboring pN categories were all statistically significant. The 5-year survival rates according to the pN status for R0 and any R resections were 75% and 75% (N0), 50% and 49% (N1), 38% and 36% (N2), and 32% and 20% (N3), respectively. The results clearly showed that pN status reflects the prognosis of patients after resection regardless of the R status (for a R0 setting: between pN0 and pN1, $p < 0.0001$; between pN1 and pN2, $p < 0.0001$; between pN2 and pN3, $p = 0.0012$ and for any R setting but adjusting for R0 status: between pN0 and pN1, $p < 0.0001$; between pN1 and pN2, $p < 0.0001$; between pN2 and pN3, $p < 0.0001$). Survival according to pN status was further analyzed within each T category (Fig. 4). For all T categories except T4 tumor, there was a difference in prognosis between neighboring pN categories. (The difference between the small number of pN3 cases and pN2 was not significant in T1, T2, or T4.) In T4, the survival curves of pN1 and pN2 overlapped during the first 2 years of follow-up, and then separated, with pN2 showing worse survival than pN1, although the difference was not significant. However, both showed significantly worse survival than pN0. Figure 5 shows the survival curves according to the pN status for the four geographical regions: Asia (n = 23,636, 79.5%), Europe (n = 2479, 8.3%), North/South America (n = 2644, 8.9%), and Australia (n = 969, 3.3%). As such, the data size submitted for this study was quite different for the four geographical regions. Regardless of the geographic location, the pN category well reflected the prognosis. However, there were important differences in 5-year survival rates according to the geographic region, especially for the pN0 and pN1 categories. The 5-year survival rates for pN0 by geographic region are 79% for Asia, 54% for Europe, 67% for North/South America, and 58% for Australia. There was a 25% difference between Asia and Europe. The 5-year survival rates for pN1 by geographic region are 54% for Asia, 34% for Europe, 48% for North/South America, and 41% for Australia. Again, there was almost a 20% difference between Asia and Europe. For higher nodal categories, the difference in survival gradually diminished.

Further analyses were performed to explore the prognostic impact of combining the present nodal categories and the number of involved lymph node stations in T-any M0 patients for whom we had complete information on pN categories. According to the number of involved lymph node stations (single versus multiple), pN categories were further subdivided: pN1 was divided into pN1 single (pN1a) and pN1 multiple (pN1b) and pN2 was divided into pN2 single (pN2a) and pN2 multiple (pN2b). The survival curves for pN1a, pN1b, pN2a, and pN2b are shown in Figure 6. Regardless

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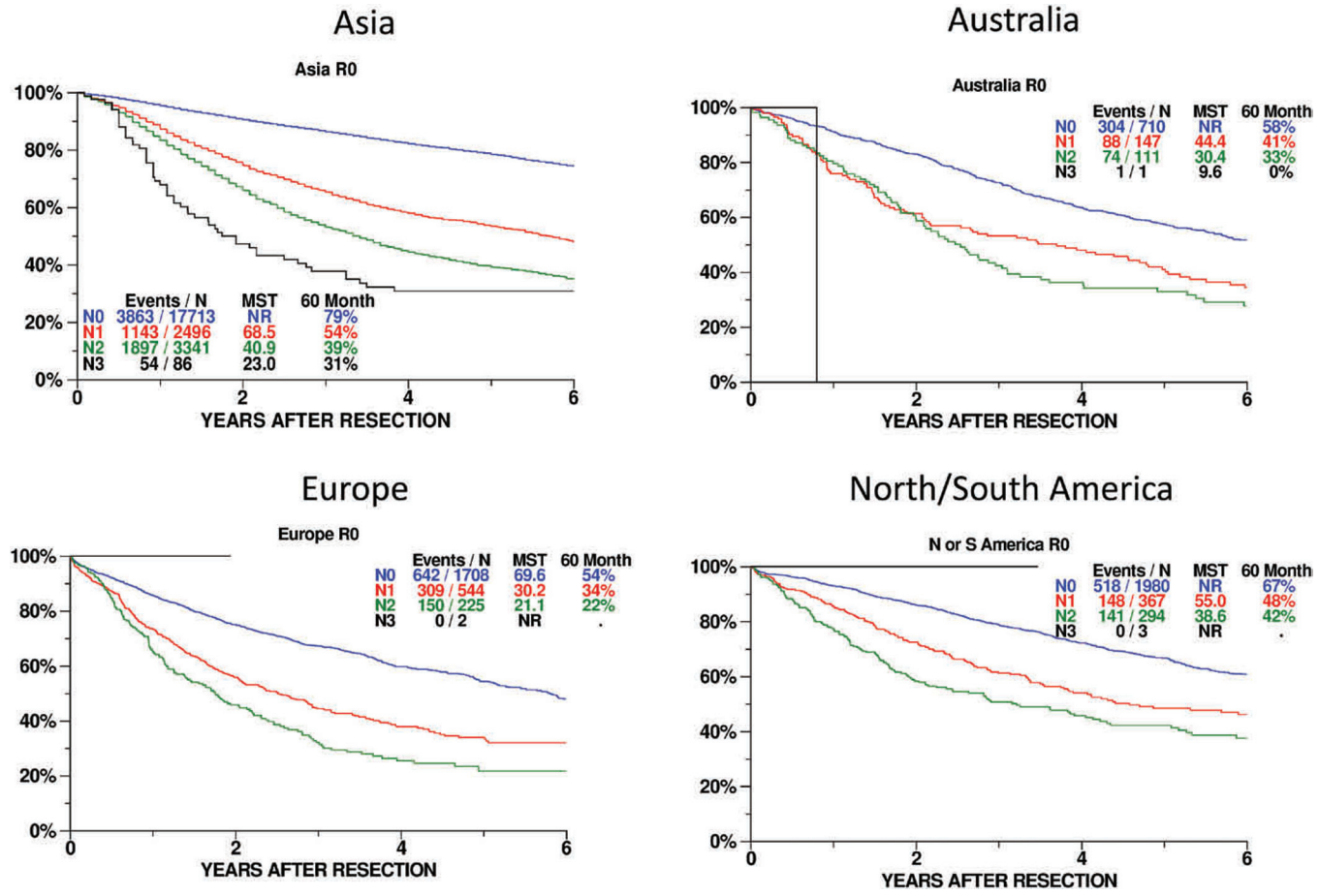
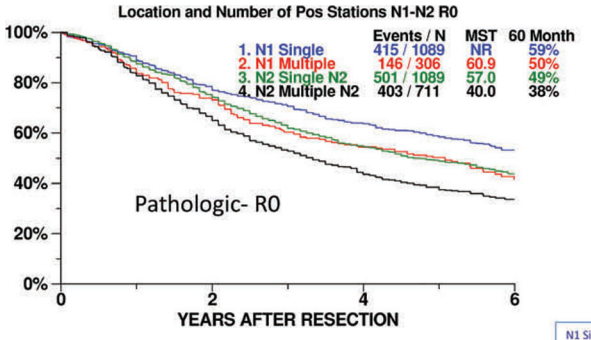
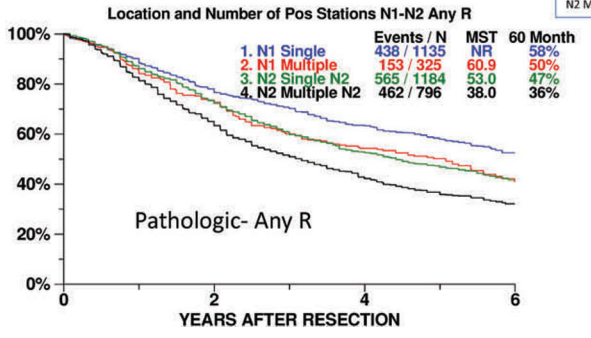


FIGURE 5. Survival curves for pN0, pN1, pN2, and pN3 T-any M0, R0 resected tumors according to geographic sources of data.



N1a vs N1b vs N2a vs N2b Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+ , and Region. (Cox PH regression on R0 cases)		
comparison	HR	P
N1b vs N1a	1.40	0.0005
N2a vs N1b	1.04	0.6798
N2b vs N2a	1.47	<.0001

N1 Single = N1a
N1 Multiple = N1b
N2 Single N2 = N2a
N2 Multiple N2 = N2b



N1a vs N1b vs N2a vs N2b Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+ , R0 resection, and Region. (Cox PH regression on All cases)		
comparison	HR	P
N1b vs N1a	1.38	0.0005
N2a vs N1b	1.08	0.4133
N2b vs N2a	1.41	<.0001

FIGURE 6. Exploratory analyses of survival in pN1 and pN2 according to the number of metastatic nodal stations (single versus multiple) for R0 and any R settings (T-any M0). The pN1 category is divided into pN1 single (N1a) and pN1 multiple (N1b). The pN2 category is further divided into pN2 single (N2a) and pN2 multiple (N2b). Despite their different categories, the survival curves for pN1b and pN2a overlap, with 5-year survival rates of 50% and 49% for R0 resection, respectively.

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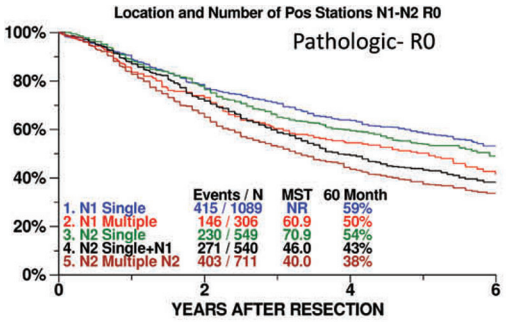
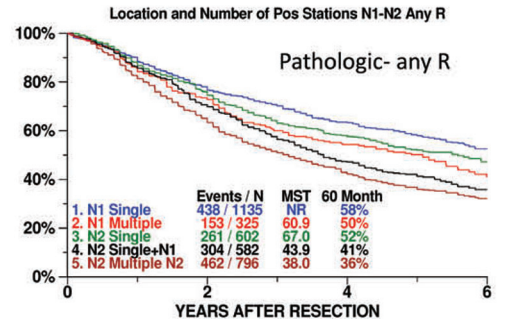
of the R status, the survival curves of pN1b and pN2a overlapped, with no difference in survival, whereas the differences between pN1a and pN1b, and between pN2a and pN2b, were statistically significant. The presence of skip metastasis was further taken into consideration: pN2a was divided into pN2 single with skip (no pN1 involvement, pN2a1), pN2 single without skip (pN1 involvement as well, pN2a2), and pN2b. The survival curves for pN1a, pN1b, pN2a1, pN2a2, and pN2b are shown in Figure 7. There was a statistically significant difference in survival between pN2a1 and pN2a2, as well as between pN2a2 and pN2b. However, there was no significant difference in prognosis between pN1b and pN2a1. These results indicated that the prognosis of pN2a1 without nodal involvement in N1 region (skip metastasis) was close to that of pN1b without nodal involvement in N2 region.

DISCUSSION

Among the three components in the TNM classification for lung cancer, the nodal component (N) is of particular concern not only to surgeons, but also to radiation oncologists and medical oncologists because metastasis to a specific lymph node site (station or zone) is an important determinant in establishing the "stage" of the patient and the optimal therapeutic modality, sometimes in combination. One of the most important issues in the thoracic oncology is how to accurately describe metastasis to locoregional lymph node stations. The 7th edition staging system defines the nodal status as N0 (no nodes involved), N1 (peribronchial, interlobar, or hilar node involvement), N2 (ipsilateral mediastinal node involvement), or N3 (contralateral mediastinal, contralateral hilar, or supraclavicular node involvement) depending solely on the location of the metastatic lymph nodes. The definition of nodal categorization was not changed in the last revision from the 6th to the 7th edition. More importantly, with regard to lung cancer, the principle has been maintained that the nodal status is based on the anatomical location of the metastatic lymph node in the thorax and not on the number of the metastatic lymph nodes (nN). Among tumors at various sites, the lung is the only site in which nodal categorization is determined by location alone, regardless of the tumor burden in the involved lymph nodes.[1,2] In other organs, the nodal status is determined according to nN (gastrointestinal tract, breast, and kidney), the combination of nN and size (head and neck), or simply the presence of regional lymph node metastasis (prostate and cervical uterus). Despite its similar location in the thoracic cavity and the fact that it shares common lymphatic pathways, nodal categorization for esophageal cancer is based solely on nN: N0, no nodal involvement; N1, metastasis in 1 and 2 lymph nodes; N2, metastasis in 3 to 6 lymph nodes; N3, metastasis in 7 or more regional lymph nodes. This principle in lung cancer has been widely accepted because the lymph node location can be easily determined on computed tomography or positron emission tomography, it is prognostic, and this categorization is anatomically reasonable from the perspective of a lymphatic pathway from the lung parenchyma through the hilum, mediastinum, and supraclavicular fossa.

The possibility of nN instead of location-based cN or pN for nodal categorization in lung cancer has been studied in the past. Wei et al.[9] and Saji et al.[10] compared the two categorizations, by location (pN) and number of metastatic lymph nodes (nN), and showed that nN is a better prognostic determinant than the location-based pN classification. Indeed, the present data also demonstrated that the prognoses of pN1 and pN2 were reversed when the number of metastatic lymph node stations and the absence/presence of skip metastasis were taken into consideration. Patients with pN2 metastasis at a single lymph node station without hilar involvement (skip metastasis) had better survival than those with pN1 metastasis at multiple





N1a vs N1b vs N2a1 vs N2a2 vs N2b Comparisons
Adjusted for Histology (adeno vs others), Sex, Age 60+ , and Region.
(Cox PH regression on R0 cases)

comparison	HR	P
N1b vs N1a	1.39	0.0005
N2a1 (skip) vs N1b	0.89	0.2863
N2a2 vs N2a1 (skip)	1.35	0.0007
N2b vs N2a2	1.26	0.0028
N2a2 vs N1b	1.21	0.064

N1 Single = N1a
N1 Multiple = N1b
N2 Single N2 ("skip mets") = N2a1
N2 Single N2 + N1 = N2a2
N2 Multiple N2 = N2b

N1a vs N1b vs N2a1 vs N2a2 vs N2b Comparisons
Adjusted for Histology (adeno vs others), Sex, Age 60+ , R0 Resection, and Region.
(Cox PH regression on All cases)

comparison	HR	P
N1b vs N1a	1.38	0.0005
N2a1 (skip) vs N1b	0.92	0.4331
N2a2 vs N2a1 (skip)	1.37	0.0002
N2b vs N2a2	1.21	0.0117
N2a2 vs N1b	1.26	0.0197

FIGURE 7. Exploratory analyses of survival for pN1 and pN2 according to the number of metastatic nodal stations (single versus multiple, skip metastasis versus nonskip metastasis) for R0 and any R settings (T-any M0). pN1 is divided into pN1 single (N1a) and pN1 multiple (N1b). The pN2 category is further divided into pN2 single with skip metastasis (N2a1), pN2 single with N1 metastasis (N2a2), and pN2-multiple (N2b). There was no statistically significant difference in survival between pN1b and pN2a1, with 5-year survival rates of 50% and 52% for R0 resection, respectively.

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stations. In the location-based categorization, the tumor burden at regional lymph nodes is not reflected at all. Thus, a small, even microscopic, metastasis at a single #10 node and gross involvement of multiple lymph nodes of 2 cm in size at stations #10 and #11 belong to the same category as N1. This might have accounted for the small inversion of the prognosis. On the other hand, Wei et al.[9] addressed the problems of nN in practical use. For example, it is quite difficult to determine nN before treatment by low-resolution imaging diagnosis. On a positron emission tomographic image, metastatic nodes are not clearly separated for accurate counting. This difficulty in counting the number of metastatic nodes directly affects the stage of the patient. Unfortunately, the present database did not include information regarding the number of involved nodes, and it was not possible for us to assess the value of nN. Information regarding the involved stations, not nodes, and thus the possibility of more accurate nodal staging was available from only a limited number of institutions. Therefore, we recommend that physicians should prospectively record both nN and the location using the IASLC nodal map and anatomical definitions for use in the future analysis. As the number of metastatic lymph nodes is used for nodal categorization in many organs, the need to collect this information should be addressed for future analysis.

The IASLC Lung Cancer Staging Project has been very successful in revising the staging system through a rigorous scientific process. However, the nature of the data needs to be addressed from a statistical perspective. As noted previously, information on the N categorization was available for 38,910 and 31,426 patients for analyses of cN and pN status, respectively. However, there was considerable imbalance in the origin of the data for the present staging project. Japan submitted the largest amount of data on N: data regarding cN for 23,012 patients (59.1%) and regarding pN for 23,463 patients (74.7%). Most of the data, especially those for pN status, came from Japan. On the other hand, only a small fraction of data, 3.6% (cN) and 8.7% (pN), came from North/South America. As noted above, two different lymph node maps were used when these databases were constructed, and the use of different maps might have caused a stage shift, with a different prognosis for the same pN status. The present analysis of N was mostly an evaluation of nodal categorization based upon Japanese-Naruke map. Therefore, it might not be appropriate to conclude that nodal categorization according to MDATS is also prognostic. We must fully understand the imbalance in the data source with respect to N to interpret these results. Future revisions should be based on a well-balanced, truly international large data set using the unified, internationally recognized nodal map developed by the IASLC and the accompanying anatomical definitions.[8] Global collaboration for the collection of well-balanced data from all over the world needs to be addressed for the future revisions.

Lastly, the method used to evaluate harvested lymph nodes needs to be standardized. It has been noted that the incomplete retrieval of lymph nodes from a resected specimen seriously affects nodal categorization.[11] According to the TNM rules, at least six lymph nodes need to be removed, three from N1 and three from N2 stations. This is the minimum requirement for a diagnosis of N0 when lymph nodes are negative.[1] However, there is still a question regarding the minimum number of lymph nodes that should be assessed pathologically. Usually, when systematic lymph node dissection is performed, the lymph nodes are dissected en bloc together with surrounding adipose tissue as a lump. Ideally, pathologists or surgeons should remove these nodes out as distinct nodes. Otherwise, some of the nodes can be missed without undergoing a pathological assessment. Future staging system should provide guidelines or suggestions regarding a standardized method for evaluating dissected/removed lymph nodes, as well as a formula for reporting.

The present analyses of the 1999 to 2010 IASLC database with respect to the N component have shown that the present N categories are still useful for distinguishing between tumors with significantly different prognoses in both clinical and pathological settings. In addition, the number of involved nodal stations was found to have prognostic impact, although this finding was derived from pathological staging and could not be validated in clinical staging. Therefore, while this finding has intrinsic value for refining the postoperative prognosis for individual patients and for creating postoperative prognostic groups, it could not be used to recommend modifications to the present N descriptors because, in principle, clinical and pathological descriptors should be the same. However, in the 7th edition of the TNM classification of malignant tumors, cancers of the breast and penis are exceptions to this rule and have different descriptors for the clinical and pathological N categories. Fixation and mobility are used for clinical staging, and the number of involved lymph nodes is used to define the pathological N categories. These two exceptions reflect the difficulty of counting the number of involved lymph nodes in clinical staging and, at the same time, acknowledge the importance of the number of involved lymph nodes at pathological staging. Because of the difficulty of counting the number of involved lymph nodes in lung cancer with the tests that are currently available for clinical staging and the unquestionable evidence that the number of involved nodes has a significant prognostic impact, we may wish to seriously consider if lung cancer should also be an exception to the rule if robust data demonstrating this can be collected.

In conclusion, based on the results of the analyses of the new IASLC database, the IASLC Staging and Prognostic Factors Committee recommends the following policy regarding the N component for the 8th edition of the TNM classification of lung cancer.

Recommendations

1. The use of the N descriptors described in the 7th edition of TNM for Lung Cancer should be carried forward, without changes into the 8th edition.
2. Additional analyses suggest that the combination of location of metastatic nodes, nN (single station versus multiple stations), and absence versus presence of skip metastasis as pN0, pN1a, pN1b, pN2a1, pN2a2, and pN2b may give a more accurate prognosis. This classification requires prospective evaluation before being considered for future revisions of the TNM staging system for lung cancer.
3. The IASLC nodal map and anatomical definitions[8] should be used to describe regional lymph node involvement for lung cancer

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APPENDIX

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